



# Validation of the EORTC Brain Cancer Module (QLQ-BN20) in Brain Metastases Patients

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# Background

- 20-40% of cancer patients will develop brain metastases during their illness
- Most common treatment is whole brain radiotherapy (WBRT): median survival 3-6 months
- Goals of WBRT:
  - Improve neurological symptoms
  - Allow tapering of steroids
  - Possibly improve survival
  - ? Maintain/Improve Quality of Life (QOL)



# Background

- Because of the short survival of brain metastases patients, consideration of **QOL** is very important
- However, there is no standard, validated QOL instrument for use in this patient population



## QOL Instruments used in Brain Metastases Clinical Trials

QOL Instrument	Frequency (# of studies)
Spitzer Quality of Life Index (SQLI)	3
Study-designed QOL assessment	2
Edmonton Symptom Assessment Scale (ESAS)	1
EORTC QLQ C30 (alone)	1
With Brain Cancer Module (BN20)	3
With Lung Cancer Module (LC13)	1
Functional Assessment of Cancer Therapy – General scale (FACT-G) (alone)	1
With Brain Subscale (FACT-Br)	5
Profile of Mood States- Short Form (POMS-SF)	1

Literature Search from 1950-2008



## QOL Instruments used in Brain Metastases Clinical Trials

QOL Instrument	Instrument Description
<b>Spitzer Quality of Life Index (SQLI)</b>	Patients with Chronic Illness *Rated by caregivers (not patients) = 3-point scale on 5 domains (activity level, activities of daily living, health, social support, & emotional state)
<b>Edmonton Symptom Assessment Scale (ESAS)</b>	Cancer Patients = 9 questions about common symptoms in cancer patients
<b>EORTC QLQ C30</b>	Cancer Patients = 30 questions: 9 multi-item scales - 1 global scale, 5 functional scales (physical, role, emotional, cognitive, and social), and 3 symptom scales (nausea, pain, fatigue). Remaining 6 questions are single items addressing other symptoms & financial impact.
Brain Cancer Module (BN20)	<b>Primary Brain Tumor</b> Patients = 20 questions to assess neurological deficits, future uncertainty, and disease- and treatment-related symptoms
Lung Cancer Module (LC13)	Lung Cancer Patients = 13 questions to assess respiratory & treatment-related symptoms
<b>Functional Assessment of Cancer Therapy – General scale (FACT-G)</b>	Cancer Patients (& other Chronic Illnesses) = 27 questions in 4 domains (physical, social/family, emotional, and functional well-being)
Brain Subscale (FACT-Br)	<b>Primary Brain Tumor</b> Patients = 23 questions to assess neurologic and cognitive deficits
<b>Profile of Mood States – Short Form (POMS-SF)</b>	Psychiatric Patients, Medical Patients, Normal Adults = 30 questions that assess 6 mood states



## QOL Instruments used in Brain Metastases Clinical Trials

QOL Instrument	# of Questions
Spitzer Quality of Life Index (SQLI)	5
Edmonton Symptom Assessment Scale (ESAS)	9
EORTC QLQ C30 (alone)	30
With <b>Brain</b> Cancer Module (BN20)	30 + 20 = 50
With Lung Cancer Module (LC13)	30 + 13 = 43
Functional Assessment of Cancer Therapy – General scale (FACT-G) (alone)	27
With <b>Brain</b> Subscale (FACT-Br)	27 + 23 = 50
Profile of Mood States- Short Form (POMS-SF)	30



# EORTC QLQ-BN20

- Used with the EORTC QLQ-C30
- QOL assessment tool for pts with primary brain tumors
- Validated in 105 pts with primary brain tumors
  - Mean age 41 years (range 18-75)
  - 41/105 were recently diagnosed
  - 64/105 had a recurrence following surgery and radiation or chemotherapy
- Has not been **validated** in brain metastases pts
- Gerrard *et al* (2003)
  - Pts struggled to complete the 50-item questionnaire
  - Poor compliance and study termination as a result



# Therefore...

- There is a need to **validate** an instrument in patients with brain metastases before application as QOL tool
- The question is...
  - Do we validate the EORTC QLQ-BN20 *or* FACT-Br?



# Proposal

- FACT-G + FACT-Br = 50 items
- EORTC QLQ-C30 + EORTC QLQ-BN20 = 50 items
- However,
  - The C30 has been shortened to produce the EORTC **QLQ-C15-PAL**
  - 15 questions validated among 41 patients and 66 health care professionals in 6 countries



## EORTC QLQ-C15-PAL (Version 1)

We are interested in some things about you and your health.

Please answer all of the questions yourself by circling the number that best applies to you.

There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

	Not at All	A Little	Quite a Bit	Very Much
1. Do you have any trouble taking a <u>short</u> walk outside of the house?	1	2	3	4
2. Do you need to stay in bed or a chair during the day?	1	2	3	4
3. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

### During the past week:

	Not at All	A Little	Quite a Bit	Very Much
4. Were you short of breath?	1	2	3	4
5. Have you had pain?	1	2	3	4
6. Have you had trouble sleeping?	1	2	3	4
7. Have you felt weak?	1	2	3	4
8. Have you lacked appetite?	1	2	3	4
9. Have you felt nauseated?	1	2	3	4





# Objective

- We propose the validation of the BN20 + **C15-PAL**
- However, 2 cognitive items were removed from the C30:

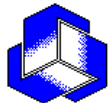
## During the past week:

	Not at All	A Little	Quite a Bit	Very Much
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4

- These will be added to the BN20, making it **BN20+2**
- Therefore, total of **37** items (vs. 50 items) assess QOL in patients with brain metastases in future trials



## EORTC QLQ–BN20 + 2 Cognitive Items



Patients sometimes report that they have the following symptoms. Please indicate the extent to which you have experienced these symptoms or problems during the past week.

<b>During the past week:</b>	<b>Not at all</b>	<b>A little</b>	<b>Quite a bit</b>	<b>Very much</b>
1. Did you feel uncertain about the future?	1	2	3	4
2. Did you feel you had setbacks in your condition?	1	2	3	4
3. Were you concerned about disruption of family life?	1	2	3	4
4. Did you have headaches?	1	2	3	4
5. Did your outlook on the future worsen?	1	2	3	4
6. Did you have double vision?	1	2	3	4
7. Was your vision blurred?	1	2	3	4
8. Did you have difficulty reading because of your vision?	1	2	3	4
9. Did you have seizures?	1	2	3	4
10. Did you have weakness on one side of your body?	1	2	3	4
11. Did you have trouble finding the right words to express yourself?	1	2	3	4
12. Did you have difficulty speaking?	1	2	3	4



## EORTC QLQ–BN20 + 2 Cognitive Items *(continued)*

Patients sometimes report that they have the following symptoms. Please indicate the extent to which you have experienced these symptoms or problems during the past week.

<b>During the past week:</b>	<b>Not at all</b>	<b>A little</b>	<b>Quite a bit</b>	<b>Very much</b>
13. Did you have trouble communicating your thoughts?	1	2	3	4
14. Have you had difficulty in <b>concentrating</b> on things, like reading a newspaper or watching television?	1	2	3	4
15. Have you had difficulty <b>remembering</b> things?	1	2	3	4
16. Did you feel drowsy during the daytime?	1	2	3	4
17. Did you have trouble with your coordination?	1	2	3	4
18. Did hair loss bother you?	1	2	3	4
19. Did itching of your skin bother you?	1	2	3	4
20. Did you have weakness of both legs?	1	2	3	4
21. Did you feel unsteady on your feet?	1	2	3	4
22. Did you have trouble controlling your bladder?	1	2	3	4



<u>Domains:</u>	<u>Number of Items</u>
future uncertainty	4
visual disorder	3
motor dysfunction	3
communication deficit	3
<u>Single items:</u>	
headaches	1
seizures	1
drowsiness	1
hair loss	1
itchy skin	1
weakness of legs	1
bladder control	1
concentration	1
memory	1

# EORTC BN20

## Scoring

BN20:

- 20 items grouped into 4 domains
- 7 single items

BN20+2:

- 2 additional single items: concentration and memory



# Methods

*Methods of questionnaire validation follow the EORTC Module Development Guidelines*

- 1) **Content validation** of the EORTC QLQ-BN20+2 and EORTC QLQ-C15-PAL in patients with brain metastases
  - Patient Interviews
  - Health Care Professional Interviews
  - Modification of BN20+2 if necessary prior to field testing
  
- 2) **Large scale field testing**
  - assess the reliability, validity, inter- and intra-subject variability, and test-retest reproducibility



# Step 1: Content Validation

## Patient Interviews

- Structured interview with each patient after completion of EORTC QLQ-C15-PAL and QLQ-BN20+2
  - Questions directed to each module item of the BN20+2 separately
  - Two questions directed to the entire questionnaire



# Content Validation

Questions for each module item:

ie) During the past week, did you have headaches?

*I see that you **have** experienced headaches in the past week. (2-4)*

Is this correct?
Can you tell me about this problem?
Do you think that this problem is related to brain metastases?
Did you have difficulty in replying to this question?
Did you find this question annoying/confusing/upsetting?
How would you have asked this question?



# Content Validation

Questions for each module item:

ie) During the past week, did you have headaches?

*I see that you **have not** experienced headaches in the past week. (1)*

Is this correct?
Have you ever experienced this problem before last week?
If yes, do you have any idea if that had something to do with brain metastases or its treatment?
If yes, can you tell me about this problem?
Did you have difficulty in replying to this question?
Did you find this question annoying/confusing/upsetting?
How would you have asked this question?



# Content Validation

Overall module questions if patient is too tired to answer for each individual item

Were there question that you found difficult to answer?
Were there questions that you found annoying?
Were there questions that you found confusing?
Were there questions that you found upsetting?
Were there questions that you found intrusive?
Do you have other comments about these questions?



# Content Validation

2 questions directed to the entire questionnaire:

- 1) Were there questions that you found irrelevant?
- 2) Can you think of additional issues that are relevant for you, but are not included in this questionnaire?



# Content Validation

## Healthcare Professional (HCP) Interviews

Asked to rank each item of the BN20+2

QUALITY OF LIFE ISSUES	i) Please indicate for each item the relevancy of it during patient illness, on a scale of (1) “not at all” to (4) “very much”.				ii) Include this item in the final questionnaire? (circle Yes or No for each item)	
	RELEVANT					
During the <u>past week</u> :	Not at All	A Little	Quite a Bit	Very Much		
1. Did you feel uncertain about the future?	1	2	3	4	Yes	No



# Content Validation

## Healthcare Professional (HCP) Interviews

- After ranking each item, asked 3 more questions:
- Please indicate which 5 to 10 issues affect the quality of life of patients with brain metastases **most profoundly**, that we should **definitely include** in the final questionnaire
- For each issue that you circled a 1 (“not at all relevant”) or 2 (“a little relevant”) **why** you consider it not or only a little relevant?
- Please let us know if you think any of the questions are **inappropriate, irrelevant, or upsetting** to patients.



# Content Validation

After patient and HCP interviews....

- **Modification** of the BN20+2 *if necessary*
  - deletion, addition, and/or modification of items according to EORTC Module Development Guidelines
- Proceed to Step 2: **Large-Scale Field-Testing:**
  - patients treated with the following modalities who were not approached in the first step:
    - A) neurosurgical resection
    - B) radiosurgery/gamma knife
    - C) WBRT
    - D) symptom management



## Step 2: Large-Scale Field Testing

Debriefing questionnaire completed by the patient after completion of EORTC QLQ-C15-PAL and QLQ-BN20+2 at initial assessment:

- **How long** did it take you to complete the QLQ-BN20+2 and QLQ-C15-PAL?
- Did you **need help** completing the assessment?
  - If “yes”, who helped you?
- Did you have **difficulty** with any of the items?
- Did you find any of the items **confusing**?
- Did you have difficulty with the **wording or phrasing** of any of the items?
- Did you find any of the items **upsetting**?
  - If “yes”, which item(s)? Explain. How would you fix this problem?



# Large-Scale Field Testing

## Follow-Up Assessment:

- EORTC QLQ-C15-PAL and QLQ-BN20+2 completed by telephone or in person (if patient has a clinic visit)
- KPS, current systemic therapy, and current/recent hospitalization will be documented

## Timing of Follow-up Assessment:

- **WBRT** and **radiosurgery/gamma knife** patients: 4-6 weeks after initial assessment
- **Symptom control** patients: 2-4 weeks after initial assessment
- **Neurosurgery** patients: 1 week after initial assessment (test-retest), and then again 4 weeks later



# Preliminary Results

## Step 1 (Content Validation): Patient Results

- Data from Feb, 2008 to present (PMH and OCC, Toronto, ON)
- N= 38 (11 males, 27 females)
- Primary Cancer Sites:
  - Lung: 20 (53%)
  - Breast: 5 (24%)
  - Others: 7(18%)
- Age:
  - Mean: 61.1 years
  - Median: 61 years
  - Range: 39-86 years
- KPS:
  - Median: 70 (30-90)
- Treatment:
  - Radiation: 19 (48%)
  - Chemotherapy: 15 (38%)
  - Surgery 4 (10%)



# Content Validation: Patient Results

BN20+2 Items	Not at all/A little (%)	Quite a bit/Very much (%)	Related to brain metastases?	
			Yes (%)	No (%)
1. Feel uncertain about the future	53	47	90	10
2. Feel had setbacks in condition	42	58	85	15
3. Concerned about disruption in family life	47	53	78	22
4. Headaches	80	20	77	14
5. Outlook on the future worsened	63	37	92	8
6. Double Vision	90	10	53	47
7. Blurred vision	83	17	63	37
8. Difficulty reading because of vision	89	11	63	37
9. Seizures	94	6	50	50
10. Weakness on one side of the body	54	46	84	16
11. Trouble finding the right words to express themselves	89	11	91	9
12. Difficulty speaking	95	5	82	18
13. Trouble communicating thoughts	96	4	81	19
14. Drowsy during the daytime	78	22	91	9
15. Difficulty remembering things	88	12	79	21
16. Feel drowsy during the daytime	73	27	65	35
17. Trouble with coordination	77	23	84	16
18. Bothered by hair loss	88	12	36	64
19. Bothered by itching of skin	82	18	67	33
20. Weakness in both legs	66	34	55	45
21. Feel unsteady on feet	40	60	74	26
22. Trouble controlling bladder	91	9	18	82



# Content Validation: Patient Results

- General Comments
  - Questionnaire was well received by most patients
- Specific Comments
  - Q1: Did you feel uncertain about the future?
    - Not related to brain metastases (n=4)
    - Uncertain about health in general (n=3)
  - Q3: Were you concerned about disruption of family life?
    - Not related to brain metastases (n=4)
    - Upsetting (n=5)
  - Q5: Did your outlook on the future worsen?
    - Upsetting (n=6)
    - Related to health and disease in general (n=4)



# Content Validation: HCP Results

n=61

<b>CENTRES/COUNTRY</b>	<b>n (%)</b>
PMH/Canada	31 (50.8%)
OCC/Canada	30 (49.2%)
<b>SEX</b>	
Female	37 (60.7%)
Male	15 (24.6%)
<b>SPECIALTY</b>	
Radiation Therapists	25 (41.0%)
Registered Nurses	13 (21.3%)
Radiation Oncologists	11 (18.0%)
Medical Oncologists	6 (9.8%)
Social Workers	4 (6.6%)
Palliative Care Physicians	2 (3.3%)



# Content Validation: HCP Results

BN20+2 Items	Not at all/A little relevant (%)	Quite a bit/Very much relevant (%)	Include in BN20+2?	
			Yes	No
1. Feel uncertain about the future	27	73	61	39
2. Feel had setbacks in condition	40	60	48	52
3. Concerned about disruption in family life	15	85	74	26
4. Headaches	3	97	89	11
5. Outlook on the future worsened	34	66	31	69
6. Double Vision	8	92	68	32
7. Blurred vision	11	89	70	30
8. Difficulty reading because of vision	14	86	54	46
9. Seizures	2	98	89	11
10. Weakness on one side of the body	3	97	83	17
11. Trouble finding the right words to express themselves	11	89	65	35
12. Difficulty speaking	7	93	81	19
13. Trouble communicating thoughts	5	95	83	17
14. Drowsy during the daytime	3	97	91	9
15. Difficulty remembering things	2	98	92	8
16. Feel drowsy during the daytime	18	82	66	34
17. Trouble with coordination	2	98	89	11
18. Bothered by hair loss	33	67	56	44
19. Bothered by itching of skin	55	45	26	74
20. Weakness in both legs	8	92	61	39
21. Feel unsteady on feet	5	95	83	17
22. Trouble controlling bladder	26	74	67	33



# Content Validation: HCP Results

## Specific Comments

- Q1: Did you feel uncertain about the future?
  - Not specific to brain metastases pts (n=4)
  - Overlaps with Q5 (n=2)
  
- Q5: Did your outlook on the future worsen?
  - Overlaps with Q1 (n=2)
  
- Q19: Did itching of the skin bother you?
  - Not a major issue expressed by pts (n=7)
  - Easy to treat (n=3)
  
- Q22: Did you have trouble controlling your bladder?
  - Uncommon manifestation in brain metastases patients (n=4)



## Content Validation: HCP Results

<b>RANK</b>	<b>Item</b>	<b>Frequency</b>
<b>1</b>	9. Seizures	38
<b>2</b>	4. Headaches	35
<b>3</b>	17. Trouble with coordination	30
<b>4</b>	21. Feel unsteady on feet	29
<b>5</b>	10. Weakness on one side of the body	29
<b>6</b>	15. Difficulty remembering things	28
<b>7</b>	12. Difficulty speaking	28
<b>8</b>	3. Concerned about disruption in family life	28
<b>9</b>	13. Trouble communicating thoughts	26
<b>10</b>	14. Difficulty concentrating on things (reading a newspapers, watching television)	22



# Next Steps

- Analysis of data for Step 1 (Content Validation) from all participating centres (including Cyrus, Greece, Hong Kong, Germany, Spain, Argentina)
- Modification of BN20+2 (if necessary)
- Proceed to Step 2 (Large-scale field testing)



# Thank-you!

Questions? Comments?

*Please contact us if you are interested in participating*

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